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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,461	11/20/2003	Albert John Molinari	WYNC-0774 (AM100978)	9854

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EXAMINER	
AULAKH, CHARANJIT	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 08/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,461	MOLINARI ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6 and 9-19* is/are rejected.

7)☒ Claim(s) *4,7 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-19 are pending in the application.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 10-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating inflammatory diseases, does not reasonably provide enablement for inhibiting inflammatory diseases or treating/inhibiting all other diseases such as psoriasis, stroke, ischemia, crohn's disease, indeterminate colitis, ulcerative colitis, reperfusion injury, sepsis, diabetes, Alzheimer disease, cognitive decline, senile dementia, hypercholesterolemia, cardiovascular disease, rstenosis etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed: Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation

necessary, the amount of direction or guidance provided, the state of the prior art, presence of working examples and the breadth of claims.

The instant compounds are shown to have anti-inflammatory activity since they inhibit NF-kB and IL-6 expression as shown by experimental in vitro data in table 1. Based on these results, the instant compounds will have utility in treating but not preventing inflammatory diseases. There is no teaching either in the specification or prior art that overexpression of NF-kB or increased production of IL-6 is implicated in the etiology of diseases other than inflammatory diseases such as psoriasis, stroke, ischemia, crohn's disease, indeterminate colitis, ulcerative colitis, reperfusion injury, sepsis, diabetes, Alzheimer disease, cognitive decline, senile dementia, hypercholesterolemia, cardiovascular disease, rstenosis etc. There is no teaching either in the specification or prior art that increased production of IL-6 is the sole mechanism responsible for the etiology of all known inflammatory diseases. It is well known in the art that there are multiple mechanisms responsible for the etiology of any known disease condition and therefore, correcting one mechanism will be able to treat but not prevent (completely cure) that particular disease condition. There are no working examples present showing efficacy of the instant compounds in known animal models of any disease condition following their in vivo administration. The instant compounds of formulae (I) and (II) encompass hundreds of thousands of compounds and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate the effectiveness of the instant compounds in known animal models of psoriasis, stroke, ischemia, crohn's disease, indeterminate colitis,

ulcerative colitis, reperfusion injury, sepsis, diabetes, Alzheimer disease, cognitive decline, senile dementia, hypercholesterolemia, cardiovascular disease, rstenosis etc. and hence their utility in treating all these disease conditions.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3, 5, 6 and 9-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claims 1 and 9, the values of variables R1-R4, R7-R12, R14 and R15 defined as --- or are taken together with either Rp+1 or Rp-1 linked with an –alkylene-, or –X-alkylene- group ---- are indefinite since sentence is incomplete and the actual intent is not clear. It appears that something is missing. Are two variables such as R1 and R2 are taken together? It is not clear what is being taken together with what and furthermore, which variable is linked to alkylene or X-alkylene group.

In independent claims 1 and 9, the values of variables R5 and R6 defined as ---may be taken together with either R6 or R7 (in case of R5) and R5 or R7 (in case of R6) and linked with an- alkylene- or –X-alkylene- group ------- are indefinite since the actual intent is not clear. It appears that something is missing.

In independent claims 1 and 9, the values of variables R21-R24, R27-R31 and R33-R35 defined as --- or are taken together with either Rq+1 or Rq-1 linked with an –

alkylene-, or –X-alkylene- group ---- are indefinite since sentence is incomplete and the actual intent is not clear. It appears that something is missing. Are two variables such as R21 and R22 are taken together? It is not clear what is being taken together with what and furthermore, which variable is linked to alkylene or X-alkylene group.

In independent claims 1 and 9, the values of variables R25 and R26 defined as ---may be taken together with either R26 or R27 (in case of R25) and R25 or R27 (in case of R26) and linked with an- alkylene- or –X-alkylene- group ------- are indefinite since the actual intent is not clear. It appears that something is missing.

In claims 10-19, the term ---inhibiting--- is indefinite since the degree of inhibition (20%, 40%, 60%, 80% or 100%) is not defined and furthermore, how this inhibition is being assessed in vivo? The applicants are suggested to delete this term.

Allowable Subject Matter

6. Claims 4, 7 and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The instant compounds are allowable over the prior art since thay are neither disclosed nor obvious over the prior art. In the prior art, Grigg (Tetrahed. Lett., cited on applicant's form 1449) discloses compound (4) on page 3859 which is closely related to instant compounds. However, the compound of Grigg differs from the instant compounds in lacking –OR13 or –OR32 substitution on the phenyl ring and furthermore,

there is no teaching, suggestion or motivation in the prior art to modify the compound of Grigg to prepare the instant compounds.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625